IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

FOUNDATION MEDICINE, INC., *Plaintiff,* v. GUARDANT HEALTH, INC., *Defendant.*	Case No. 2:16-cv-00523-JRG-RSP

CLAIM CONSTRUCTION MEMORANDUM OPINION AND ORDER

Before the Court is the opening claim construction brief of Foundation Medicine, Inc. ("Plaintiff") (Dkt. No. 72, filed on April 6, 2017),[1] the response of Guardant Health, Inc. ("Defendant") (Dkt. No. 77, filed on April 20, 2017), and the reply of Plaintiff (Dkt. No. 80, filed on April 27, 2017). The Court held a hearing on the issues of claim construction and claim definiteness on May 18, 2017. Having considered the arguments and evidence presented by the parties at the hearing and in their briefing, the Court issues this Order.

[1] Citations to the parties' filings are to the filing's number in the docket (Dkt. No.) and pin cites are to the page numbers assigned through ECF.

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I. BACKGROUND

Plaintiff alleges infringement of U.S. Patent No. 9,340,830 (the "'830 Patent). The '830 Patent is entitled "Optimization of Multigene Analysis of Tumor Samples." The application leading to the '830 Patent was filed on December 29, 2011 and the patent issued on May 17, 2016. The '830 Patent claims priority to a number of provisional applications filed between December 30, 2010 and October 28, 2011.

In general, the '830 Patent is directed to methods for optimizing genetic analysis of tumor samples. The basic method includes acquiring a set of genetic material from a tumor sample ("acquiring a library"), using bait sets tailored to target tumor material to enrich the collected set with respect to the targeted material ("contacting the library" with the bait sets "to provide selected tumor members"), and sequencing the tumor material of the enriched set to determine genetic characteristics of the tumor mutation.

The abstract of the patent provides:

> A method of analyzing a tumor sample comprising: (a) acquiring a library comprising a plurality of tumor members from a tumor sample; (b) contacting the library with a bait set to provide selected members; (c) acquiring a read for a subgenomic interval from a tumor member from said library; (d) aligning said read; and (e) assigning a nucleotide value (e.g., calling a mutation) from said read for the preselected nucleotide position, thereby analyzing said tumor sample.

Claims 1 and 65, the patent's independent claims, recite as follows:

> **1.** A method of analyzing a tumor sample for a somatic mutation, comprising:
> (a) acquiring a library comprising a plurality of tumor members from the tumor sample;
> (b) contacting the library with at least two bait sets to provide selected tumor members, wherein said bait sets hydridize with the tumor members, thereby providing a library catch;
> (c) sequencing by a next generation sequencing method a subgenomic interval comprising the somatic mutation from a tumor member from said library or library catch, thereby acquiring a read for the subgenomic interval;
> (d) aligning said read by an alignment method; and
> (e) assigning a nucleotide value from said read for a preselected nucleotide position, thereby analyzing said tumor sample,

wherein the at least two bait sets of step (b) are chosen from two of the following bait sets:

(i) a first bait set that selects a high-level target chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample;

(ii) a second bait set that selects a mid-level target chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 10% or higher of the cells from the tumor sample;

(iii) a third bait set that selects a low-level target chosen from one or more nucleic acid molecules that comprise a subgenomic interval chosen from one or more of:

a) a pharmacogenomic (PGx) single nucleotide polymorphism (SNP) that distinguishes the ability of a patient to metabolize different drugs,

b) a plurality of genomic SNPs that uniquely identify (fingerprint) a patient, or

c) a genomic SNP or locus that is used to assess copy number gains or losses of genomic DNA and loss-of-heterozygosity (LOH);

(iv) a fourth bait set that selects a nucleic acid molecule that comprises an intron sequence that detects a structural breakpoint; or

(v) a fifth bait set that selects a one-copy deletion of several terminal exons, wherein each bait set of said plurality has a unique preselected efficiency for selection for its target as compared with the other bait sets in the plurality.

65. A method of analyzing a tumor sample for a somatic mutation, comprising:

(a) acquiring a library comprising a plurality of tumor members from the tumor sample;

(b) contacting the library with at least two bait sets to provide selected tumor members, wherein said bait sets hybridize with the tumor members, thereby providing a library catch;

(c) sequencing by a next generation sequencing method a subgenomic interval comprising the somatic mutation from a tumor member from said library catch, thereby acquiring a read for the subgenomic interval; thereby analyzing said tumor sample for the somatic mutation,

wherein the at least two bait sets of step (b) are chosen from two of the following bait sets:

(i) a first bait set that selects a high-level target chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample;

(ii) a second bait set that selects a mid-level target chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 10% or higher of the cells from the tumor sample;

(iii) a third bait set that selects a low-level target chosen from one or more nucleic acid molecules that comprise a subgenomic interval chosen from one or more of:
a) a pharmacogenomic (PGx) single nucleotide polymorphism (SNP) that distinguishes the ability of a patient to metabolize different drugs,
b) a plurality of genomic SNPs that uniquely identify (fingerprint) a patient, or
c) a genomic SNP or locus that is used to assess copy number gains or losses of genomic DNA and loss-of-heterozygosity (LOH);
(iv) a fourth bait set that selects a nucleic acid molecule that comprises an intron sequence that detects a structural breakpoint; or
(v) a fifth bait set that selects a one-copy deletion of several terminal exons,
wherein each bait set of said plurality has a unique preselected efficiency for selection for its target as compared with the other bait sets in the plurality.

II. LEGAL PRINCIPLES

A. Claim Construction

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting *Innova/Pure Water Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). To determine the meaning of the claims, courts start by considering the intrinsic evidence. *Id.* at 1313; *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 861 (Fed. Cir. 2004); *Bell Atl. Network Servs., Inc. v. Covad Commc'ns Group, Inc.*, 262 F.3d 1258, 1267 (Fed. Cir. 2001). The intrinsic evidence includes the claims themselves, the specification, and the prosecution history. *Phillips*, 415 F.3d at 1314; *C.R. Bard, Inc.*, 388 F.3d at 861. The general rule—subject to certain specific exceptions discussed *infra*—is that each claim term is construed according to its ordinary and accustomed meaning as understood by one of ordinary skill in the art at the time of the invention in the context of the patent. *Phillips*, 415 F.3d at 1312–13; *Alloc, Inc. v. Int'l Trade Comm'n*, 342 F.3d 1361, 1368 (Fed. Cir. 2003); *Azure Networks, LLC v. CSR PLC*, 771 F.3d 1336, 1347 (Fed. Cir. 2014) ("There is a heavy presumption

that claim terms carry their accustomed meaning in the relevant community at the relevant time.") (vacated on other grounds).

"The claim construction inquiry … begins and ends in all cases with the actual words of the claim." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998). "[I]n all aspects of claim construction, 'the name of the game is the claim.'" *Apple Inc. v. Motorola, Inc.*, 757 F.3d 1286, 1298 (Fed. Cir. 2014) (quoting *In re Hiniker Co.*, 150 F.3d 1362, 1369 (Fed. Cir. 1998)). First, a term's context in the asserted claim can be instructive. *Phillips*, 415 F.3d at 1314. Other asserted or unasserted claims can also aid in determining the claim's meaning, because claim terms are typically used consistently throughout the patent. *Id.* Differences among the claim terms can also assist in understanding a term's meaning. *Id.* For example, when a dependent claim adds a limitation to an independent claim, it is presumed that the independent claim does not include the limitation. *Id.* at 1314–15.

"[C]laims 'must be read in view of the specification, of which they are a part.'" *Id.* (quoting *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc)). "[T]he specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'" *Id.* (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325 (Fed. Cir. 2002). But, "'[a]lthough the specification may aid the court in interpreting the meaning of disputed claim language, particular embodiments and examples appearing in the specification will not generally be read into the claims.'" *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quoting *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571 (Fed. Cir. 1988)); *see also Phillips*, 415 F.3d at 1323. "[I]t is improper to read limitations from a preferred embodiment described in the specification—even if

it is the only embodiment—into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 913 (Fed. Cir. 2004).

The prosecution history is another tool to supply the proper context for claim construction because, like the specification, the prosecution history provides evidence of how the U.S. Patent and Trademark Office ("PTO") and the inventor understood the patent. *Phillips*, 415 F.3d at 1317. However, "because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* at 1318; *see also Athletic Alternatives, Inc. v. Prince Mfg.*, 73 F.3d 1573, 1580 (Fed. Cir. 1996) (ambiguous prosecution history may be "unhelpful as an interpretive resource").

Although extrinsic evidence can also be useful, it is "'less significant than the intrinsic record in determining the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc.*, 388 F.3d at 862). Technical dictionaries and treatises may help a court understand the underlying technology and the manner in which one skilled in the art might use claim terms, but technical dictionaries and treatises may provide definitions that are too broad or may not be indicative of how the term is used in the patent. *Id.* at 1318. Similarly, expert testimony may aid a court in understanding the underlying technology and determining the particular meaning of a term in the pertinent field, but an expert's conclusory, unsupported assertions as to a term's definition are not helpful to a court. *Id.* Extrinsic evidence is "less reliable than the patent and its prosecution history in determining how to read claim terms." *Id.* The Supreme Court recently explained the role of extrinsic evidence in claim construction:

> In some cases, however, the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for

> example, the background science or the meaning of a term in the relevant art during the relevant time period. *See, e.g., Seymour v. Osborne*, 11 Wall. 516, 546 (1871) (a patent may be "so interspersed with technical terms and terms of art that the testimony of scientific witnesses is indispensable to a correct understanding of its meaning"). In cases where those subsidiary facts are in dispute, courts will need to make subsidiary factual findings about that extrinsic evidence. These are the "evidentiary underpinnings" of claim construction that we discussed in *Markman*, and this subsidiary factfinding must be reviewed for clear error on appeal.

Teva Pharm. USA, Inc. v. Sandoz, Inc., 135 S. Ct. 831, 841 (2015).

B. Departing from the Ordinary Meaning of a Claim Term

There are "only two exceptions to [the] general rule" that claim terms are construed according to their plain and ordinary meaning: "1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of the claim term either in the specification or during prosecution."[2] *Golden Bridge Tech., Inc. v. Apple Inc.*, 758 F.3d 1362, 1365 (Fed. Cir. 2014) (quoting *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012)); *see also GE Lighting Solutions, LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014) ("[T]he specification and prosecution history only compel departure from the plain meaning in two instances: lexicography and disavowal."). The standards for finding lexicography or disavowal are "exacting." *GE Lighting Solutions*, 750 F.3d at 1309.

To act as his own lexicographer, the patentee must "clearly set forth a definition of the disputed claim term," and "clearly express an intent to define the term." *Id.* (quoting *Thorner*, 669 F.3d at 1365); *see also Renishaw*, 158 F.3d at 1249. The patentee's lexicography must appear "with reasonable clarity, deliberateness, and precision." *Renishaw*, 158 F.3d at 1249.

[2] Some cases have characterized other principles of claim construction as "exceptions" to the general rule, such as the statutory requirement that a means-plus-function term is construed to cover the corresponding structure disclosed in the specification. *See, e.g., CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1367 (Fed. Cir. 2002).

To disavow or disclaim the full scope of a claim term, the patentee's statements in the specification or prosecution history must amount to a "clear and unmistakable" surrender. *Cordis Corp. v. Boston Sci. Corp.*, 561 F.3d 1319, 1329 (Fed. Cir. 2009); *see also Thorner*, 669 F.3d at 1366 ("The patentee may demonstrate intent to deviate from the ordinary and accustomed meaning of a claim term by including in the specification expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope."). "Where an applicant's statements are amenable to multiple reasonable interpretations, they cannot be deemed clear and unmistakable." *3M Innovative Props. Co. v. Tredegar Corp.*, 725 F.3d 1315, 1326 (Fed. Cir. 2013).

C. Definiteness Under 35 U.S.C. § 112, ¶ 2 (pre-AIA) / § 112(b) (AIA)[3]

Patent claims must particularly point out and distinctly claim the subject matter regarded as the invention. 35 U.S.C. § 112, ¶ 2. A claim, when viewed in light of the intrinsic evidence, must "inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129 (2014). If it does not, the claim fails § 112, ¶ 2 and is therefore invalid as indefinite. *Id.* at 2124. Whether a claim is indefinite is determined from the perspective of one of ordinary skill in the art as of the time the application for the patent was filed. *Id.* at 2130. As it is a challenge to the validity of a patent, the failure of any claim in suit to comply with § 112 must be shown by clear and convincing evidence. *Id.* at 2130 n.10. "[I]ndefiniteness is a question of law and in effect part of claim construction." *ePlus, Inc. v. Lawson Software, Inc.*, 700 F.3d 509, 517 (Fed. Cir. 2012).

[3] The Court refers to the pre-AIA version of § 112 but understands that there is no substantial difference between definiteness under the pre-AIA version and under the AIA version of the statute.

III. AGREED CONSTRUCTIONS

The parties have agreed to the following constructions set forth in their Joint Claim Construction Chart Pursuant to Patent Local Rule 4-5 (Dkt. No. 82).

Term[4]	Agreed Construction
preamble Claim 1	preamble is limiting
preamble Claim 65	preamble is limiting
"tumor member" • Claims 1, 65	"a member having a sequence from a tumor cell"
"member" • Claims 1, 65	"a nucleic acid molecule that is in a library"
"sample" • Claims 1, 65	"a collection of similar cells obtained from a tissue, or circulating cells, of a subject or patient"
"tumor sample" • Claims 1, 65	"a sample that includes tumor cells" • "tumor cells" means "cells possessing characteristics typical of cancer-causing cells, such as uncontrolled proliferation, immortality, metastatic potential, rapid growth and proliferation rate, and certain characteristic morphological features"
"library" • Claims 1, 65	"a collection of members"
"subgenomic interval" • Claims 1, 65	"a portion of a genomic sequence"
"coverage depth" • Claims 2, 66	"the average number of sequencing reads that align to a base or bases in a reference nucleotide sequence"

Having reviewed the intrinsic and extrinsic evidence of record, the Court hereby adopts the parties' agreed constructions.

[4] For all term charts in this order, the claims in which the term is found are listed with the term but: (1) only the highest-level claim in each dependency chain is listed, and (2) only asserted claims identified in the parties' Joint Claim Construction Chart Pursuant to Patent Local Rule 4-5 (Dkt. No. 82) are listed.

IV. CONSTRUCTION OF DISPUTED TERMS

A. "bait set that selects a high-level target," "bait set that selects a mid-level target," and "bait set that selects a low-level target"

Disputed Term	Plaintiff's Proposed Construction	Defendant's Proposed Construction
"bait set that selects a high-level target" • Claims 1, 65	No construction necessary because it is self-defined in Claims 1 and 65.	bait set tailored to capture a target for which the deepest coverage is required
"bait set that selects a mid-level target" • Claims 1, 65	No construction necessary because it is self-defined in Claims 1 and 65.	bait set tailored to capture a target for which high coverage is required
"bait set that selects a low-level target" • Claims 1, 65	No construction necessary because it is self-defined in Claims 1 and 65.	bait set tailored to capture a target for which low-medium coverage is required

Because the parties' arguments and proposed constructions with respect to these terms are related, the Court addresses the terms together.

The Parties' Positions

Plaintiff submits these terms are defined in the claims and therefore do not need to be construed. Dkt. No. 72 at 9. Specifically, Plaintiff contends a "high-level target" is defined in the claims as:

> chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample.

Id. at 10 (citing '830 Patent col.227 ll.39–43 (Claim 1), col.239 ll.18–22 (Claim 65)). A "mid-level target" is defined in the claims as:

> chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 10% or higher of the cells from the tumor sample.

Id. (citing '830 Patent col.227 ll.44–48 (Claim 1), col.239 ll.23–27 (Claim 65)). A "low-level target" is defined in the claims as:

> chosen from one or more nucleic acid molecules that comprise a subgenomic interval chosen from one or more of: a) a pharmacogenomic (PGx) single nucleotide polymorphism (SNP) that distinguishes the ability of a patient to metabolize different drugs, b) a plurality of genomic SNPs that uniquely identify (fingerprint) a patient, or c) a genomic SNP or locus that is used to assess copy number gains or losses of genomic DNA and loss-of-heterozygosity (LOH).

Id. (citing '830 Patent col.227 ll.49–59 (Claim 1), col.239 ll.28–38 (Claim 65)). Thus the terms are defined according to the targeted mutation frequency or type. *Id.* at 11, 13.

Plaintiff argues that Defendant's proposed "deepest coverage," "high coverage," and "low-medium coverage" language should be rejected because this language is used in the patent to describe exemplary embodiments of the targets rather than to define the targets. *Id.* at 11–14. This language, Plaintiff further argues, cannot be definitional else there is no difference between the target of the third bait set and the target of the fourth bait set, which are both described as targets "for which low-medium coverage is needed." *Id.* at 14 (quoting '830 Patent col.13 ll.41–44, 53–55).

In addition to the claims themselves, Plaintiff cites the following intrinsic and extrinsic evidence to support its position: **Intrinsic evidence**: '830 Patent col.13 ll.20–55. **Extrinsic evidence**: Gabriel Decl.[5] ¶¶ 25–26, 32, 39 (Plaintiff's Ex. 2, Dkt. No. 72-2 at 9, 12, 14–15).

Defendant responds that—as described in the patent and during prosecution—each bait-set is tailored to optimize the sensitivity to the target mutation and the tailoring is accomplished through varying the sequencing coverage depth for the target. Dkt. No. 77 at 8–15. Because this tailoring was used to overcome an examiner's § 101 rejection and the only tailoring described in the patent is the sequencing coverage depth, the bait sets are limited by the coverage depth as

[5] Initial Declaration of Stacey Gabriel, Ph.D. in Support of Foundation Medicine, Inc.'s Proposed Claim Constructions.

described in the patent. *Id.* at 10–14. The coverage-depth limitations are in addition to the recited mutation-frequency and mutation-type limitations recited in the claims. *Id.* at 14–15.

In addition to the claims themselves, Defendant cites the following **intrinsic evidence** to support its position: '830 Patent col.13 ll.20–25, col.13 ll.30–35, col.13 ll.41–45, col.67 l.66 – col.68 l.14, col.68 ll.20–25, col.93 ll.59–63, col.94 ll.5–9, col.94 ll.18–21; '830 Patent File Wrapper July 16, 2015 Office Action (Defendant's Ex. 5, Dkt. No. 77-5), December 16, 2015 Amendment in Response to Non-Final Office Action Under 37 C.F.R. § 1.111 (Defendant's Ex. 2, Dkt. No. 77-2), December 16, 2015 Declaration Under 37 C.F.R. § 1.132 (Defendant's Ex. 3, Dkt. No. 77-3), April 4, 2016 Notice of Allowance and Fee(s) Due (Defendant's Ex. 4, Dkt. No. 77-4).

Plaintiff replies that while the bait sets of the claims are tailored to the target mutations, the claims themselves specify the tailoring. Dkt. No. 80 at 5–7. For example, the first bait set is tailored to select a target "chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample." *Id.* at 6.

Analysis

The dispute here distills to what meaning should be given to "high-level," "mid-level," and "low-level," as those terms modify "target" in the claim. Plaintiff essentially argues that "high-level," "mid-level," and "low-level" are redundant. Defendant argues that "high-level," "mid-level," and "low-level" refer to the sequencing depth coverage required by the target. The Court understands "high-level," "mid-level," and "low-level" differentiate the bait sets on the relative sequencing-depth coverage—the coverage for the high-level target is higher (deeper) than the coverage for the mid-level target which is higher than the coverage for the low-level target.

The parties agree that the bait sets are each tailored to specific targets. Indeed, the patentee argued—successfully—that the tailored nature of the bait sets takes the invention out of the unpatentable realm of the abstract. *See, e.g.*, '830 Patent File Wrapper December 16, 2015 Amendment in Response to Non-Final Office Action Under 37 C.F.R. § 1.111 at 34 ("In providing for detection of alterations across multiple classes of genomic alterations in a single assay utilizing these tailored bait sets, the methods of the claims represent significantly more than an abstract idea and, in fact, an important advancement in genomic analysis in oncology.") (Dkt. No. 77-2 at 35); '830 Patent File Wrapper April 4, 2016 Notice of Allowance and Fee(s) Due at 3 ("The instant invention is an improvement to a particular technology of cancer genomic testing by optimizing the conditions for detection of somatic mutations through the use of tailored bait sets followed by next generation sequencing of the resulting library catch.") (Dkt. No. 77-4 at 9). The statements in the prosecution history comport with the description in the patent. *See, e.g.*, '830 Patent col.12 ll.64–67 ("The methods and compositions disclosed herein provide different bait sets for achieving different depths and patterns of coverage for complex target nucleic acid sequences (e.g., nucleic acid libraries)."), col.94 ll.45–47 ("The methods and compositions featured in the invention involve tuning the relative sequence coverage of each bait set/target category.").

The patent teaches that a bait set is tailored to a target based on the efficiency of selection for the target. *See, e.g.*, '830 Patent col.11 ll.25–35. The "efficiency of selection" is defined in the patent as: "the level or depth of sequence coverage as it is adjusted according to a target subgenomic interval(s)." *Id.* at col.11 ll.32–35. And the "level of sequencing depth" is defined as "the level of coverage of reads (e.g., unique reads), after detection and removal of duplicate reads." *Id*. at col.12 ll.43–46.

There is no evidence that "high-level target," "mid-level target," and "low-level target" have an ordinary and customary meaning in the art. Indeed, the only evidence of record on this issue suggests the contrary. Gabriel Decl. ¶ 25 ("The term 'high-level target,' standing alone, does not clearly connote a specific frequency or a specific level of coverage required to capture the nucleic acid molecules comprising the somatic mutation."), ¶ 32 ("The term 'mid-level target,' standing alone, does not clearly connote a specific frequency or a specific level of coverage required to capture the nucleic acid molecules comprising the particular somatic mutation."), ¶ 39 ("The term 'low-level target,' standing alone, does not clearly connote a specific frequency or a specific level of coverage required to capture particular nucleic acid molecules.") (Dkt. No. 72-2 at 9, 12, 14).

As used in the patent, "high-level," "mid-level," and "low-level" are used to define targets based on the relative sequence coverage required by the targets. As stated in the patent, "[t]he methods and compositions featured in the invention involve tuning the ***relative*** sequence coverage of each bait set/target category." '830 Patent col.94 ll.45–47 (emphasis added). The bait set for a "high-level target" is tuned (or "tailored") to "select[] a high-level target … for which the deepest coverage is required to enable a high level of sensitivity for an alteration … that appears at a low frequency." *Id*. at col.13 ll.20–25; *see also*, *id*. at col.67 ll.66 – col.68 l.4, col.93 l.59 – col.94 l.4. The bait set for a "mid-level target" is tailored to "select[] a mid-level target … for which high coverage is required to enable high level of sensitivity for an alteration … that appears at a higher frequency than the high-level target." *Id*. at col.13 ll.30–36; *see also*, *id*. at col.68 ll.9–15, col.94 ll.5–10. Likewise, the bait for a low-level target is tailored to "select[] a low-level target … for which low-medium coverage is required to enable high level of sensitivity." *Id*. at col.13 ll.41–45; *see also*, *id*. at col.68 ll.20–24, col.94 ll.18–21. Thus, the high-level target corresponds to that

target of the three requiring the deepest coverage and the low-level target corresponds to that target of the three requiring the shallowest coverage. The terms "high-level," "mid-level," and "low-level" are used to denote a hierarchy of required coverage. The Court's understanding comports with the of that of the parties' experts. *See* Gabriel Dep. 34:12 – 35:7, 38:11–15 (testifying that the high-level target of the claims requires a deeper level of coverage than the mid-level target and that Defendant's proposed "coverage" language is not inconsistent with the claims, it is "just not necessary") (Dkt. No. 77-1 at 11–12); Quackenbush Decl. ¶ 65 ("the claims recite bait sets in which their unique efficiencies of selection will cause them to enrich lower frequency targets to a greater extent, resulting in deeper sequencing coverage, and vice versa") (Dkt. No. 72-3 at 30).

The Court rejects Plaintiff's proposed construction for two reasons. First, it does not capture that the bait sets are tailored to the target, as explained in the prosecution history and patent. The tailoring is related to how efficiently the target is selected, not just whether it is selected. This is not clear from the claim language alone. And second, it does not give any effect to "high-level," "mid-level," and "low-level," contravening the well-established canon that "[c]laims must be interpreted with an eye toward giving effect to all terms in the claim." *Info-Hold, Inc. v. Muzak LLC*, 783 F.3d 1365, 1373 (Fed. Cir. 2015).

The Court rejects Defendant's proposed construction because it does not unambiguously convey the hierarchy of sequencing coverage denoted by the "high-level," "mid-level," and "low-level" labels. Further, Defendant's proposed construction threatens to render the relative nature of these coverage terms into an absolute measure. Indeed, at oral argument, Defendant argued exactly this. Defendant then contended that "deepest coverage," "high coverage," and "low-medium coverage"—as used in the patent to describe the high-level, mid-level, and low-level targets—are terms of art denoting specific coverage ranges that should be read into the claims. However,

Defendant has not presented any evidence that these terms carry such a meaning or, if they do, what coverage ranges are encompassed by these terms. While the patent describes various exemplary coverage ranges, the descriptions are exemplary and are not definitional. *See, e.g.*, '830 Patent col.13 l.1 – col.14 l.62, col.66 l.21 – col.69 l.40, col.93 l.57 – col.94 l.44. And specific sequencing-depth ranges are recited in dependent Claim 48, belying Defendant's contention that "high-level target" "mid-level target," and "low-level target" are necessarily associated with specific coverage ranges. *Id*. at col.237 ll.26–48.

The Court is not persuaded by Defendant's oral argument that construing "high-level target," "mid-level target," and "low-level target" to denote a relative hierarchy of coverage would render the claims indefinite. According to Defendant: (1) the second bait set allows for mutation frequencies over 10%, therefore the bait set may be tailored to a frequency of 100%, (2) the coverage for a mutation frequency of 100% is the minimum coverage, and (3) the third bait set could not, therefore, have a shallower coverage than the second bait set. But whether a particular bait set is tailored to the relative coverage of the "high-level target," "mid-level target," or "low-level target" is an issue of infringement, not of claim scope.

Accordingly, the Court construes the "high-level target," "mid-level target," and "low-level target" terms, with surrounding claim language for context, as follows:

- "[first] bait set that selects a high-level target [chosen from]" means "[first] bait set tailored to select a target requiring deeper coverage than the target of the second bait set, the target [chosen from]";
- "[second] bait set that selects a mid-level target [chosen from]" means "[second] bait set tailored to select a target requiring shallower coverage than the target of the first bait set, the target [chosen from]"; and

- "[third] bait set that selects a low-level target [chosen from]" means "[third] bait set tailored to select a target requiring shallower coverage than the target of the second bait set, the target [chosen from]."

B. "wherein each bait set of said plurality has a unique preselected efficiency for selection for its target as compared with the other bait sets in the plurality"

Disputed Term	Plaintiff's Proposed Construction	Defendant's Proposed Construction
"wherein each bait set of said plurality has a unique preselected efficiency for selection for its target as compared with the other bait sets in the plurality" • '830 Patent Claim 1, 65	wherein at least two bait sets have distinct preselected efficiencies for selecting their targets	see "preselected" and "efficiency for selection"
"preselected" • '830 Patent Claim 1, 65	No construction necessary.	selected prior to performing the method
"efficiency for selection" • '830 Patent Claim 1, 65	No construction necessary.	level of depth of sequence coverage as it is adjusted to a target subgenomic interval(s)

Because the parties' arguments and proposed constructions with respect to these terms are related, the Court addresses the terms together.

The Parties' Positions

Plaintiff submits the entire "wherein" clause should be construed, and not just "preselected" and "efficiency for selection." Dkt. No. 72 at 15. Plaintiff contends that "wherein each bait set of said plurality" refers to each of the "at least two bait sets of step (b)" that are selected from the recited bait sets. *Id.* at 16. Plaintiff further contends that each of these two selected bait sets "has a unique preselected efficiency for selection for its target as compared with other baits sets in the plurality" in that each of the selected bait sets has a preselected efficiency that is distinct from the preselected efficiencies of the other selected bait sets. *Id.*

In addition to the claims themselves, Plaintiff cites the following intrinsic and extrinsic evidence to support its position: **Intrinsic evidence**: '830 Patent col.3 ll.51–52, col.11 l.66 – col.12 l.3, col.66 ll.57–59. **Extrinsic evidence**: Gabriel Decl. ¶¶ 45–49, 51–52 (Plaintiff's Ex. 2, Dkt. No. 72-2 at 17–19); Quackenbush Decl.[6] ¶ 66 (Plaintiff's Ex. 3, Dkt. No. 72-3 at 30).

Defendant responds that only "efficiency for selection" and "preselected," and not the entire wherein clause, need to be construed. Dkt. No. 77 at 15. According to Defendants, "efficiency for selection" is defined in the '830 Patent. *Id.* (citing '830 Patent col.11 ll.33–35). And there is no dispute that "preselected" means "selected prior to performing the method." *Id.* at 15–16. The other language of the wherein clause, Defendant contends, is clear without construction—it means "[e]ach bait set in the plurality must have a 'unique' preselected efficiency of selection 'as compared with the other bait sets in the plurality.'" *Id.* at 16. Defendant further argues that Plaintiff's proposed construction would improperly encompass multiple selected bait sets that have the same "efficiency for selection" so long as at least two of the selected bait sets had distinct efficiencies. *Id.* at 16–17.

In addition to the claims themselves, Defendant cites the following intrinsic and extrinsic evidence to support its position: **Intrinsic evidence**: '830 Patent col.11 ll.33–35. **Extrinsic evidence**: Gabriel Dep.[7] 91:1–8, 91:16–20, 92:15–19, 93:15–23, 97:11–16 (Defendant's Ex. 1, Dkt. No. 77-1 at 25–26).

Plaintiff replies that the claims only require that at least two bait sets have distinct efficiencies for selection, not that every bait set used in the method have a distinct efficiency. Dkt. No. 80 at 8–9.

[6] Expert Declaration of John Ouackenbush, Ph.D.
[7] Deposition of Stacey Gabriel, Ph.D., March 24, 2017.

Plaintiff cites further **extrinsic evidence** to support its position: Gabriel Dep. 95:8–10, 96:2–4, 97:1–4 (Defendant's Ex. 1, Dkt. No. 77-1 at 26).

Analysis

The primary issue in dispute is whether each bait set necessarily has a unique efficiency for selection or only two bait sets necessarily have efficiencies for selection that are distinct from each other. The Court understands that each of the "at least two bait sets" contacting the library have efficiencies for selection that are distinct from every other of the at least two bait sets contacting the library. That is, of the set of chosen bait sets contacting the library, each bait set within the contacting set has a unique efficiency of selection within that contacting set. "Preselected" has its plain and ordinary meaning, which is as Defendant proposes. And "efficiency for selection" means the same as "efficiency of selection," which is defined in the patent as Defendant proposes.

To begin, Plaintiff does not directly dispute Defendant's proposed constructions of "preselected" and "efficiency for selection." Rather, Plaintiff contends that construction is unnecessary when a term's "meaning is clear or when the parties agree on its meaning." Dkt. No. 80 at 8 n.5. It is not clear whether the parties do in fact agree on the meaning of "preselected" and "efficiency for selection." In any event, the Court understands the plain and ordinary meaning of "preselected" to mean "selected prior to performing the method." And the Court understands that "efficiency for selection" is used in the patent interchangeably with "efficiency of selection." *See, e.g.*, '830 Patent col.14 ll.17–23. "Efficiency of selection" is defined to mean "the level or depth of sequence coverage as it is adjusted according to a target subgenomic interval(s)." *Id*. at col.11 ll.32–35. Plaintiff's expert similarly understands these claim terms. Gabriel Dep. 90:16 – 92:19 (Dkt. No. 77-1 at 25).

According to the plain meaning of the claim language, the uniqueness requirement applies to those tailored bait sets that are chosen and used to contact the library. For example, Claim 1 recites "(b) contacting the library with at least two bait sets … wherein the at least two bait sets of step (b) are chosen from two of the following bait sets … wherein each bait set of ***said plurality*** has a unique preselected efficiency for selection for its target as compared with the other bait sets in the plurality." '830 Patent col.227 ll.24–25, ll.37–38, ll.64–67 (emphasis added). The Court understands "said plurality" refers back to the "at least two bait sets of step (b)." But this does not mean, as Plaintiff contends, that "at least two bait sets have distinct preselected efficiencies." Rather, each of the bait sets chosen from the candidate set and used to contact the library—"the at least two bait sets of step (b)"—have unique efficiencies with respect to each other. Plaintiff's expert agrees. Gabriel Dep. 93:3 – 97:25 (Dkt. No. 77-1 at 26–26).

Accordingly, the Court construes these terms as follows:

- "wherein each bait set of said plurality has a unique preselected efficiency for selection for its target as compared with the other bait sets in the plurality" means "wherein each bait set of the at least two bait sets of step (b) has a unique preselected efficiency for selection for its target as compared with the other bait sets in the at least two bait sets of step (b)";
- "preselected" means "selected prior to performing the method"; and
- "efficiency for selection" means "level or depth of sequence coverage as it is adjusted according to a target subgenomic interval(s)."

C. "somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample" and "somatic mutation that appears at a frequency of about 10% or less of the cells from the tumor sample"

Disputed Term	Plaintiff's Proposed Construction	Defendant's Proposed Construction
"somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample" • '830 Patent Claims 1, 65	Not indefinite.	Indefinite.
"somatic mutation that appears at a frequency of about 10% or less of the cells from the tumor sample" • '830 Patent Claims 1, 65	Not indefinite.	Indefinite.

Because the parties' arguments and proposed constructions with respect to these terms are related, the Court addresses the terms together.

The Parties' Positions

Plaintiff submits that these terms do not require advance knowledge of "the frequency at which a particular mutation will occur" in a particular tumor, as posited by Defendant's expert. Dkt. No. 72 at 18–20. Rather, according to Plaintiff, it is impossible to have such knowledge in advance. *Id.* at 20–21. Thus, the meaning posited by Defendant's expert would improperly render the claims inoperable. *Id.* at 22–23. These terms refer to a capability of the bait set—the bait sets "must be capable of detecting any mutations within a target that may appear at the claimed frequencies." *Id.* at 21–22.

In addition to the claims themselves, Plaintiff cites the following **extrinsic evidence** to support its position: Gabriel Decl. ¶¶ 54–55 (Plaintiff's Ex. 2, Dkt. No. 72-2 at 20–21); Gabriel Rebuttal Decl.[8] ¶¶ 9, 12–17 (Plaintiff's Ex. 5, Dkt. No. 72-5 at 7–10); Quackenbush Decl. ¶¶ 70–

[8] Rebuttal Declaration of Stacey Gabriel, Ph.D. in Support of Foundation Medicine, Inc.'s Proposed Claim Constructions.

86, 90–91 (Plaintiff's Ex. 3, Dkt. No. 72-3 at 32–41); Quackenbush Dep.[9] 157:17 – 159:25, 162:2–14 (Plaintiff's Ex. 4, Dkt. No. 72-4 at 3–6); Quackenbush IPR Decl.[10].

Defendant responds that the claims require the high-level-target and mid-level-target bait sets to be tailored to known mutation frequencies in the sample but it is impossible to know the targeted mutation frequencies before tailoring the bait sets. Dkt. No. 77 at 18–29. Thus, it is impossible to know whether a particular method is within the scope of the claims until the method is completed and therefore the claims are indefinite. *Id.* at 18–21. Further, Defendant contends, whether the method is practiced depends not only on the claim limitations but also on the patient. A method when practiced on one patient may infringe the claims while when practiced on a different patient may not, simply because of the patients' tumor characteristics. *Id.* at 21–22. Defendant contends that the testimony of Plaintiff's expert confirms the indefiniteness of the claims. *Id*. at 25–29.

In addition to the claims themselves, Defendant cites the following intrinsic and extrinsic evidence to support its position: **Intrinsic evidence**: '830 Patent col.13 ll.20–36, col.63 l.40 – col.64 l.27. **Extrinsic evidence**: Gabriel Dep. 39:10–25, 40:9–20, 41:10–22, 43:3–8, 45:9–11, 46:9–14, 48:3–12, 48:23 – 49:1, 82:1–23, 82:25 – 83:3, 91:1–20, 99:1 – 101:2, 104:2 – 105:1, 109:14–19 (Defendant's Ex. 1, Dkt. No. 77-1 at 12–14, 23, 25, 27–29); Quackenbush Decl. ¶¶ 59–65, 72–73, 76–81 (Plaintiff's Ex. 3, Dkt. No. at 72-3 at 25–30, 33–38); Gabriel Rebuttal Decl. ¶ 17 (Plaintiff's Ex. 5, Dkt. No. 72-5 at 10).

[9] Deposition of John Quackenbush, Ph.D., March 28, 2017 (excerpts).
[10] *Guardant Health Inc. v. Foundation Medicine, Inc.*, IPR2017-01170, Guardant Ex. 1002: Declaration of Dr. John Quackenbush (Claims 65, 66, 72, 73, 75–77, 80–85) (P.T.A.B. March 30, 2017).

Plaintiff replies that each bait set recited in Claims 1 and 65 is designed to capture a particular target as expressed in the claims. Dkt. No. 80 at 10. Whether that target, as defined in the claims, is present in the tumor sample is irrelevant to infringement. *Id.* at 10–11. This, according to Plaintiff, is how its expert testified. *Id*. at 12–14.

Plaintiff cites further **extrinsic evidence** to support its position: Gabriel Decl. ¶ 57 (Plaintiff's Ex. 2, Dkt. No. 72-2 at 22); Gabriel Rebuttal Decl. ¶ 20 (Plaintiff's Ex. 5, Dkt. No. 72-5 at 11); Gabriel Dep. 21:3–5, 22:11–12, 32:1–6, 45:3–14, 46:13–14, 47:8–12, 63:10 – 64:7, 67:17–21, 80:12 – 81:6, 81:18–19, 82:9–16 (Defendant's Ex. 1, Dkt. No. 77-1 at 7–8, 10, 13–14, 18–19, 22–23).

Analysis

The dispute here distills to whether the claims require pre-analysis knowledge of the frequency of the somatic mutation in the sample to be analyzed. The Court does not understand the patent to require information that the parties and their experts agree is scientifically impossible to know. Rather, the claims require baits tailored to capture targets having specific mutation characteristics if those targets are present in the tumor sample. That is, performing the analysis of the claimed method yields information regarding the characteristics of the tumor material, it is not based on this information. Defendant has failed to prove that these terms render any claim indefinite.

To begin, and as set forth above, the Court notes that the bait sets of the invention are tailored to detect the recited tumors. This denotes more than mere capability to detect a mutation. Each bait set is tailored for a distinct target coverage relative to the other chosen bait sets. *See, e.g.*, '830 Patent col.12 ll.64–67 ("The methods and compositions disclosed herein provide different bait sets for achieving different depths and patterns of coverage for complex target nucleic

acid sequences (e.g., nucleic acid libraries)."), col.55 ll.35–37 ("The bait sets can be designed from reference sequences, such that the baits are optimal for selecting targets of the reference sequences."), col.94 ll.45–47 ("The methods and compositions featured in the invention involve tuning the relative sequence coverage of each bait set/target category.").

The baits sets are tailored (designed) to perform a certain way under certain conditions, regardless of whether those conditions are actually encountered. That is, each of the baits sets have a specific capability defined by the function the bait set performs in certain conditions. For example, the first bait set "selects a high-level target chosen from one or more tumor nucleic acid molecules that comprise a subgenomic interval comprising a somatic mutation that appears at a frequency of about 5% or less of the cells from the tumor sample." *Id*. at col.227 ll.39–43. This does not require the bait set to actually select the recited target or the target mutation to actually appear at the recited frequency. Indeed, the claim expressly contemplates that this bait set may not even be chosen to contact the library. *Id*. at col.227 ll.24–27, 37–67. If, however, the first bait set is chosen to contact the library and the library includes the target tumor member, the bait set will select that target to achieve the recited relative coverage. Defining a structure, here, the bait set, by the function it performs in certain conditions is acceptable—and connotes capability to perform the function rather than requiring actual performance of the function. *UltimatePointer, v. Nintendo Co.*, 816 F.3d 816, 826–28 (Fed. Cir. 2016) (holding claims definite because the functional "limitation reflects the capability of [the] structure"); *LifeNet Health v. LifeCell Corp.*, 837 F.3d 1316, 1326–27 (Fed. Cir. 2016) ("Functional limitations recited in the negative may describe a capability or structural element.").

Further, the Court will not interpret the claim language to require something the parties and their experts agree is scientifically impossible. "As a legal matter, of course, a construction that

renders the claimed invention inoperable should be viewed with extreme skepticism." *Atlas IP, LLC v. St. Jude Med., Inc.*, 804 F.3d 1185, 1189 (Fed. Cir. 2015) (quotation marks omitted). Here, it is undisputed that "it is not possible to have foreknowledge of the frequency at which a specific mutation may occur in a specific patient's tumor before it is even tested." Dkt. No. 72 at 21; Dkt. No. 77 at 20; *see also*, Quackenbush Decl. ¶ 70 ("Thus, there is no way of knowing how frequently a mutation may occur in an individual patient's tumor until that is empirically determined."), ¶ 73 ("it is impossible to know ahead of time what the mutation frequencies in any patient may be, or whether the frequencies may be changing over time") (Dkt. No. 72-3 at 32–34); Gabriel Rebuttal Decl. ¶ 12 ("Dr. Quackenbush is correct that one cannot know in advance the frequency of a particular mutation in a tumor sample."), ¶ 15 ("However, prior knowledge of the frequency of a particular mutation in a given sample is neither possible nor necessary to perform the claimed method of the '830 patent.") (Dkt. No. 72-5 at 7, 9); Gabriel Dep. 104:2–7. Thus, Defendant's indefiniteness argument is based on a claim-construction that "should be viewed with extreme skepticism." Indeed, given that the '830 Patent is directed to optimizing genetic analyses of tumor samples, it strains credibility to presume that the optimized analysis requires foreknowledge of information that is a product of genetic analysis of the tumor. Accordingly, the Court finds Defendant's expert is not credible on this issue and rejects his presumed construction.

The bait sets here are distinguishable from the fragile-gel limitation held to render claims indefinite in *Halliburton Energy Services, Inc. v. M-I LLC*, 514 F.3d 1244 (Fed. Cir. 2008). In *Halliburton*, the term "fragile gel" rendered claims indefinite because the "fragile" nature of the gel depended on unspecified parameters that were variable within the intended environment of the claims (oil wells):

> an artisan would not know from one well to the next whether a certain drilling fluid was within the scope of the claims because a wide variety of factors could affect

> adequacy (formation geology, wellbore size, depth, angle, etc.). In other words, a given fluid might be adequate to suspend drill cuttings in some formations and/or well configurations, whereas in others it would not be.

Id. at 1254–55. The claim language at issue here, in contrast, specifies the parameters—the mutation frequencies. While the parties do not dispute that mutation frequencies vary from sample to sample, the issue is whether that variance impacts the scope of the claims. It does not. Whether a bait is tailored for the recited mutation frequency does not depend on the whether the sample includes the mutation at the recited frequency. Thus, claim scope—and infringement—is a function of the bait set, not of the sample. One of ordinary skill in the art would know whether a certain bait set was within the scope of the claims based on the mutation-frequency design specification regardless of the wide variety of factors that could affect the mutation frequency in the sample.

Accordingly, the Court finds that Defendant has not proven any claim to be indefinite.

V. CONCLUSION

The Court adopts the constructions above for the disputed and agreed terms of the ’830 Patent and holds that Defendant has failed to prove any claim is invalid as indefinite. Furthermore, the parties should ensure that all testimony that relates to the terms addressed in this Order is constrained by the Court’s reasoning. However, in the presence of the jury the parties should not expressly or implicitly refer to each other’s claim construction positions and should not expressly refer to any portion of this Order that is not an actual construction adopted by the Court. The references to the claim construction process should be limited to informing the jury of the constructions adopted by the Court.

SIGNED this 19th day of May, 2017.

ROY S. PAYNE
UNITED STATES MAGISTRATE JUDGE